REMARKS

Status of the Claims

Claim 1 has been amended. The applicants are assuming that the amendment made in the response filed on December 5, 2005 has been entered because the Advisory Action dated December 21, 2005 did not have box 3 checked, which would have indicated that the amendment was not entered. Claims 1, 10, 25-32 are pending in the present application and under examination. Claims 7, 9, 13, 15, 17, 19, 21, 23-24, and 33 are withdrawn and claims 2-6, 8, 11-12, 14, 16, 18, 20, and 22 are canceled.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Applicants thank the Examiner for indicating in the Advisory Action dated December 21, 2005 that the rejection of Claims 1, 10 and 25-32 under 35 U.S.C. § 112, second paragraph, has been withdrawn.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph (New Matter)

Claims 1 and those dependent therefrom have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants traverse the rejection and its supporting remarks. As discussed in the response filed on December 5, 2005, the applicants respectfully assert that the specification provides support for the presently pending claim 1. The specification clearly indicates on page 2, lines 7-9, that:

> "***The invention also provides polypeptides*** that are homologous (i.e., have sequence identity) to these fragments [referring to the peptides in Table I which includes SEQ ID NO:1331]. Depending on the particular fragment, the degree of sequence identity is preferably greater than 50% (e.g., 60%, ***70%***, 80%, 90%, 95%, 99% or more)." (emphasis added)

The invention clearly includes polypeptides that have 70% sequence identity to the proteins fragments including SEQ ID NO:1331, as is presently claimed and clearly support a claim to "a polypeptide comprising a contiguous amino acid sequence with at least 70% sequence identity of SEQ ID NO:1331."

Furthermore, the invention also clearly includes the purified form of such polypeptides. The specification on page 2, lines 18-22, clearly states that:

> "***The proteins of the invention*** [e.g., such as the claimed polypeptides] can, of course be prepared by various means (e.g., recombinant expression, ***purification from cell culture***, chemical synthesis, etc.) and in various forms (e.g. native, C-terminal and/or N-terminal fusions *etc.*) They are preferably prepared in substantially pure form (i.e., substantially free from other Neisserial or host cell proteins). Short proteins are preferably produced using chemical peptide synthesis." (emphasis added).

One of skill in the art would readily recognize that purification from cell culture would result in a purified polypeptide as is presently claimed as would chemical peptide synthesis. Furthermore, one of skill in the art would understand that proteins are polypeptides and therefore this section of the specification indicates that the polypeptide as claimed may be purified. Thus, the specification clearly conveys to one of skill in the art that the inventors had possession of "a ***purified*** polypeptide comprising a contiguous amino acid sequence with at least ***70% sequence identity*** to the sequence of SEQ ID NO:133," as is presently claimed.

The specification also provides support for the recitation "at least one antigenic determinant that elicits an immune response against Neisserial meningitidis strain B ..." The specification on page 3, lines 20-27, indicates that:

> "The invention provides nucleic acid, protein, or antibody according to the invention for use as medicaments (e.g., as vaccines or as immunogenic compositions) or as diagnostic reagents. It also provides the use of nucleic acid, ***protein***, or antibody ***according to the invention*** [e.g., such as the claimed purified polypeptides] in the

> manufacture of: ... (iii) ***a reagent which can raise antibodies against Neisserial bacteria.***" (emphasis added)

One of skill in the art would recognize that a polypeptide that may be used as a reagent which can raise antibodies against Neisserial bacteria would have "at least one antigenic determinant that elicits an immune response against Neisserial bacteria," as is presently claimed. In order to raise antibodies, a polypeptide must have an antigenic determinant that the antibody will bind to. Antibodies are a hallmark of an immune response, so if a polypeptide can raise antibodies, it can elicit an immune response. Therefore the present claim 1 does not include new matter.

The Examiner asserts that page 2, lines 18-22 and page 3, lines 20-27 which discuss additional characteristics of the "proteins" of the invention do not apply to the "polypeptides" discussed on page 2, lines 5-7. The MPEP clearly states that there is no requirement that claims find exact word-for-word support in the specification. See, e.g., MPEP 2163.02 ("The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the written description requirement"). Thus it is irrelevant that the language in the claims and the different sections of the specification are not word-for-word matches to each other. One of skill in the art would understand from the specification that the inventor had possession of the present claim 1, especially given that proteins are polypeptides.

Furthermore, the originally filed claims support the applicants assertion that "protein" as used on page 2, lines 18-22 and page 3, lines 20-27 included the polypeptide discussed on page 2, lines 5-7. The originally filed claims are a part of the specification and therefore can provide written description support for the presently filed claims. Originally filed claim 12 recites:

> The use of the fragment of claim 1, claim 2 or claim 3, **the polypeptide of claim 5**, the protein of claim 8, the antibody of claims 7, and/or the nucleic acid of claim 9, in the manufacture of ... (a) reagent which can raise antibodies against Neisserial bacteria. (emphasis added)

Originally filed claim 5 recited: "A polypeptide having 50% or greater sequence identity to the fragment of any preceding claim." Claim 5 is very similar to the language of page 2, lines 5-7

and claim 12 is very similar to the language of page 3, lines 20-27. Thus, claim 12 makes clear that "protein" as discussed on page 3, lines 20-27 and page 2, lines 18-22 includes polypeptides.

Therefore the applicants respectfully request that the Examiner withdraw the rejection of Claim 1 and the claims that depend therefrom based upon 35 U.S.C. § 112, first paragraph (new matter).

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1, 10 and 25-32 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not reasonably providing enablement for a polypeptide that has a length of 20, 35, 50, or 100 amino acids or less and comprises a contiguous amino acid sequence with "at least 70% sequence identity to SEQ ID NO: 1331," wherein the polypeptide comprises at least one antigenic determinant "that elicits an immune response against Neisserial meningitidis strain B," as claimed.

Applicants traverse the rejection and its supporting remarks. The Examiner has asserted that the claims are not enabled due to an alleged lack of specific guidance, lack of enabling disclosure, art demonstrated functional unpredictability, breadth of the claims, and the quantity of experimentation.

1. Breadth

The Examiner has asserted that the limitation "Neisserial bacteria" is too broad because it covers many species. The applicants respectfully disagree; however, in order to facilitate prosecution without surrendering the right to pursue broader claims, the applicants have amended the claim to recite that the immune response will be elicited against *Neisserial meningitidis* strain B. Thus, the claims are more limited in scope such that the immune response that is elicited is further defined.

2. Art demonstrated unpredictability

The Examiner has stated that "[t]he 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the effect of a change within the subject matter to which the claimed invention pertains." However, this statement cannot mean that one of skill in the art must be able to predict the exact sequence of every protein or polypeptide within the claim scope to be predictable as asserted by the Examiner. The Examiner rejected the applicants' attempt to rebut this assertion through analogy to monoclonal antibodies by merely stating that the claims are to polypeptides that elicit an immune response rather than to monoclonal antibodies. However, this argument misses the essential point that the applicants are trying to make, which is that the standard of enablement for claims to polypeptides cannot be that one of skill in the art must be able to predict *a priori* the sequence of every polypeptide within the claimed function with one hundred percent accuracy. If this were the standard, then a claim to "a monoclonal antibody that binds to a protein of SEQ ID NO:X" would not be enabled because it is indisputable that no one of skill in the art could predict the sequence of every antibody that could meet the claimed function much less the sequence of even one antibody that would bind a given protein. A claim to a monoclonal antibody that binds a specified protein is in the class of claims to a polypeptide that has a particular function, since a monoclonal antibody is a peptide and binding to a specific protein is the function of the monoclonal antibody. The Federal Circuit in *In re Wands*, was asked whether a claim to a method using HBsAg monoclonal antibody was enabled when the application only provided one example of a working monoclonal antibody from the 1F8 hybridoma that was deposited and therefore accessible to the public. The trial court held the broad claims to use of HBsAg monoclonal antibodies were not enabled by the single monoclonal antibody disclosed, but the Federal Circuit reversed the trial court's holding. If the Examiner's statement of predictability were the standard for enablement, the trial court would have been correct because one of skill in the art could not predict with one hundred percent accuracy all changes to the antibody from the 1F8 hybridoma that could be made and still have an antibody that binds HBsAg, much less all the other antibodies that could be identified by screening hybridoma. The Federal Circuit held that the broad claim to using HBsAg monoclonal antibodies was enabled even though only one working monoclonal antibody

was provided because there was a method that would predictably produce monoclonal antibodies within the scope of the claim, i.e., HBsAg monoclonal antibodies. Thus, the Wands factor relating to predictability does not mean that one of skill in the art can predict the exact sequence of every protein (such as a monoclonal antibody) or a polypeptide that is within the scope of a claim. The Wands factor relating to predictability is therefore satisfied when there is a routine protocol that will predictably produce the claimed protein or polypeptide commensurate in scope. The Federal Circuit held that the methods of generating monoclonal antibodies were in fact routine and would produce the HBsAg monoclonal antibodies needed to make and use the claimed invention. This case is similar to the present claimed invention. The application discloses the one sequence (SEQ ID NO:1331) much like Wands disclosed one HBsAg monoclonal antibody hybridoma. There are routine procedures for making the claimed polypeptides and screening for the claimed function of eliciting an immune response in *Neisserial meningitidis* strain B as discussed by the applicants in the previous response on page seven.

In addition, even if one of skill in the art cannot predict *a priori* what polypeptides fall under the scope of the present claims, there are routine methods available to test whether any particular polypeptide meets the functional limitation. Thus the present claims are enabled because there are routine methods of screening will predictably identify polypeptides with the claimed and one of ordinary skill in the art will not need to conduct undue experimentation to determine whether a polypeptide falls within the claim scope.

3. Amount of guidance

The Examiner has asserted that the present application lacks sufficient specific guidance; however, this is only relevant if the Examiner's statement of predictability is accurate, i.e., one of skill in the art must be able to predict *a priori* with complete accuracy which polypeptides have the claimed function. However, as discussed under 2 above, the predictability relates to whether there are screening methods that will predictably identify polypeptides with the claimed function. It is well established that guidance relating to routine methods need not be provided if they are readily

available to one of skill in the art. See, *e.g.*, MPEP 2164.01 "A patent need not teach, and preferably omits, what is well known in the art."

Even still, the application does provide specific guidance as to preferred fragments as described on page 37, lines 8-29 and pages 64-71 which disclose preferred fragments of 114-1 (SEQ ID NO:1331). Further, as noted on page 18-19 of the response filed June 21, 2005, the specification also provides general guidance to those of skill in the art. By "lack of enabling disclosure," the applicants assume that the Examiner is referring to working examples; however, working examples are not required to enable an invention. See, *e.g.*, In re Borkowski, 422 F.2d 904, 908 (CCPA 1970).

4. Quantity of experimentation required

The quantity of experimentation is not undue because the synthesis of peptides is routine as is the screening of the peptides against 114-1 polyclonal antibodies to demonstrate whether the polypeptides are capable of eliciting an immune response against the *Neisserial mengitidis* strain B as discussed in the previous response on page seven. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858, F.2d 731 (Fed. Cir. 1988). It is worth noting that the Federal Circuit in *In re Wands* held that "in the monoclonal antibody art it appears that an 'experiment' is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen. This process entails immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 858, F.2d at 740. Similarly, the "experiment" of identifying polypeptides that fall within the scope of the claim involves design and synthesis of a family of peptides of a particular sequence and then screening for the ability to elicit an immune response against *Neisserial meningitidis* strain B. The Federal Circuit in *In re Wands* noted that, "[p]ractitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." 858,

F.2d at 740. It therefore does not matter that one of skill in the art may have to screen more than one polypeptide to find one with the ability to elicit an immune response. Thus, while the screening of polypeptides may take time much as screening for monoclonal antibodies, the screening is all routine, so the quantity of experimentation is not undue.

5. *Relative skill of those in the art*

The skill in the art with respect to the presently claimed invention is quite high. The presently claimed polypeptides are typically isolated by research scientists who are at least Ph.D. level with a fair amount of post-doctoral experience or relevant industry experience. Thus, those of skill in the art are highly capable individuals with a high degree of familiarity with the screening methods needed to identify the claimed invention.

Thus, the claims are not unduly broad. Just as in *In re Wands*, the present application is directed to a polypeptide with a claimed function. The monoclonal antibodies in *In re Wand*, would actually have much greater sequence variation than the seventy percent identity as is presently claims. The Federal Circuit held that claims that included the HBsAg monoclonal antibody were enabled because there was a routine "experiment" to screen through hybridomas to identify monoclonal antibodies that had the claimed function of binding HBsAg. Similarly, the presently claimed invention may be practiced by routine screening methods that will produce the claimed polypeptides. Furthermore, given that the skill in the art is high just as in *In re Wands*, and the breadth of the present claims is narrower than *In re Wands*, the amount of experimentation is not undue. Therefore the present claims are enabled because making and using the claimed polypeptides would not require undue experimentation.

The applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 10 and 25-32 based upon 35 U.S.C. § 112, first paragraph, enablement.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is

determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

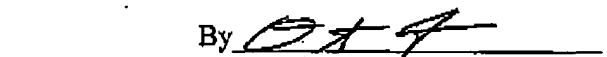
Please direct all further written communications regarding this application to:

Alisa Harbin
Chiron Corporation
Intellectual Property – R440
P.O. Box 8097
Emeryville, CA 94662-8097
Tel: (510) 923-3004
Fax: (510) 655-3542

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **223002100200**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: April 4, 2006

Respectfully submitted,

By 

Otis Littlefield
Registration No.: 48,751
MORRISON & FOERSTER LLP
425 Market Street
San Francisco, California 94105-2482
(415) 268-6846

sf-2104198